Selenium-containing Heterocycles from Isoselenocyanates: Use of Hydrazine for the synthesis of 1,3,4-Selenadiazine derivatives

Sommen, G L ; Linden, Anthony ; Heimgartner, H

Abstract: Aryl isoselenocyanates 1 react with different phenacyl halides 2 in the presence of hydrazine hydrate in a one-pot reaction to give selenadiazines 3a–3f in good-to-excellent yields.

DOI: https://doi.org/10.1002/hlca.200690131

Prof. Dr. H. Heimgartner
Tel. 01 635 4282
Fax 01 635 6836
e-mail: heimgart@oci.unizh.ch

Selenium-Containing Heterocycles from Isoselenocyanates: Use of Hydrazine for the Synthesis of 1,3,4-Selenadiazine Derivatives

by **Geoffroy L. Sommen**[1]), **Anthony Linden**, and **Heinz Heimgartner***

Organisch-Chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

Keywords: Isoselenocyanates, Selenadiazines, Cyclization reactions, Hydrazine, X-Ray crystallography

[1]) Postdoctoral stay at the University of Zürich (08.2004 – 08.2005); present address: Lonza AG, CH-3930 Visp, Switzerland.

Aryl isoselenocyanates **1** react with different phenacyl halides **2** in the presence of hydrazine hydrate in a one-pot reaction to give selenadiazines **3a-f** in good to excellent yields.

1. Introduction. – Selenium-containing heterocycles are of remarkable interest because of their antitumor, antibacterial and other notable biological and pharmaceutical activities [1]. Among our efforts devoted to the chemistry of selenium in organic synthesis, we were also interested in the preparation of selenadiazines. Several articles deal with the synthesis of 1,3,4- [2–4], 1,3,5- [5][6], and 1,2,6-selenadiazines [7] but, to the best of our knowledge, no synthesis has been described starting from isoselenocyanates. Some selenadiazines are of biological and physical interest and are found to be cardiotonic [8] or spasmolytic agents [9], but they are also of importance as agrochemicals, dyes and organic electric conductors [10].

In numerous articles, the synthesis of 1,3,4-selenadiazine derivatives by ring enlargement of other selenium-containing heterocycles like selenadiazoles or selenazoles is described [11][12]. However, most of the papers showed the uses of the selenoureas [13], selenosemicarbazides [14][15] or phenyl acetylene selenide as intermediates [16].

As a part of our program aimed at the development of simple new procedures for the synthesis of selenium-containing heterocycles [17–24], we have recently reported on the utility of isoselenocyanates as building blocks for the synthesis of 1,3-selenazetidines [25], 1,3-selenazolidines and perhydro-1,3-selenazines [26], 2-methylidene-1,3-selenazolidine derivatives [27], and 1,3-selenazepanes [28]. As an extension of this work, we report here on a novel and efficient synthesis of 1,3,4-selenadiazines.

2. Results and Discussion. – The used isoselenocyanates **1a**–**1e** (see *Tab. 1*) have been prepared conveniently by a slightly modified procedure of *Barton et al.* [29] from the corresponding *N*-arylformamide by treatment with $COCl_2$ and elemental Se. Then, hydrazine hydrate was added to a mixture of equimolar amounts of **1** and a phenacyl halide

2 in CH_2Cl_2 at room temperature. After stirring for 3–4 h, the reaction was complete (TLC) and the solvent was evaporated. The product was purified by column chromatography on silica gel using a mixture of hexane and AcOEt (ratio from 1/0 to 1/1) and recrystallized from AcOEt. The IR-spectra (KBr) of the pale-yellow solids showed two characteristic strong absorptions at *ca.* 1590 and 1560 cm^{-1} but no C=O absorption. The NMR-spectra revealed the presence of an NH (11.3–11.8 ppm) and a CH_2 group (3.8–3.95 (^{1}H) and *ca.* 15 ppm (^{13}C)), and the CI-MS and elemental analyses were in accordance with the structure of a 3,6-dihydro-2-imino-2*H*-1,3,4-selenadiazine **3** or its 2-amino tautomer (*Scheme 1*). Finally, the structure of **3a** was established by X-ray crystallography (*Figure*).

Scheme 1

Figure. ORTEP *Plot* [30] *of the molecular structure of* **3a** (arbitrary numbering of the atoms, 50% probability ellipsoids)

In the heterocyclic ring, the unsubstituted C-atom is a CH_2 group, and only one ring N-atom carries an H-atom. The other one is involved in a C=N bond. The heterocyclic ring has a distorted boat conformation. The NH group forms an intermolecular H-bond with the exocyclic imine N-atom of a neighboring molecule. In turn, the acceptor molecule makes an identical H-bond to the original molecule so that pairs of molecules are linked into centrosymmetric dimeric units. The H-bonding can be described by a graph set motif [31] of $R^2_{,2}(8)$.

The described one-pot reaction of **1**, **2**, and hydrazine led to the products **3a**–**3f** in 55–80% yield (*Table 1*). Several attempts have been made to carry out this three-component

reaction in two consecutive steps. The treatment of **1** with hydrazine hydrate, followed by the addition of a phenacyl halide **2**, did not yield the desired product, but the corresponding selenosemicarbazide was formed. On the other hand, the reaction of the hydrazone, which had been prepared from **2** and hydrazine, with **1** led quickly to decomposition products.

Table 1: *Preparation of Selenadiazines* **3** *from Isoselenocyanates* **1**

Based on the results described, we propose the reaction mechanism shown in *Scheme 2* for the formation of **3**. We have already demonstrated that isoselenocyanates **1** and bifunctional nucleophiles of type **4**, bearing an electrophilic group, react to give 2-iminoselenaheterocycles **6**. A likely intermediate is the adduct **5**, which undergoes an *exo-trig* cyclization [32] to yield five to seven-membered selenaheterocycles [26–28] or heterocyclic selones [33][34]. In the present three-component reaction, the nucleophile (hydrazine) and the electrophile (**2**) are separated. Addition of hydrazine to **1** leads to the adduct **7**, which immediately reacts with the third component **2** to give **8**. Finally, an intramolecular condensation by elimination of H_2O, *i.e.*, the formation of a hydrazone, leads to the selenaheterocycles **3**.

Scheme 2

In conclusion, we have shown that the three-component reaction of isoselenocyanates **1**, phenacyl halides **2**, and hydrazine is a very convenient and useful procedure for the preparation of 1,3,4-selenadiazines **3**.

We thank the analytical units of our institute for spectra and analyses. Financial support of this work by the *Dr. Helmut Legerlotz Foundation* and *F. Hoffmann-La Roche AG,* Basel, is gratefully acknowledged.

Experimental Part

1. *General*. TLC: silica gel *60* F_{254} plates (0.25 mm; *Merck*). Column chromatography (CC): silica gel *60* (0.040-0.063 mm; *Merck*). M.p.: *Büchi B-540* apparatus, in capillaries; uncorrected. IR spectra: *Perkin-Elmer 1600-FT-IR* spectrometer, in KBr; absorptions in cm^{-1}. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75.5 MHz) spectra: *Bruker ARX-300* instrument, in (D_6)DMSO; chemical shifts in ppm, *J* in Hz; multiplicities of C-atoms from DEPT spectra. EI-MS and CI-MS: *Finnigan SSQ-700* or *MAT-90* instrument; EI mode: 70 eV; CI mode: NH_3 as carrier gas.

2. *Starting materials*. α-Halogeno acetophenones and hydrazine hydrate are commercially available (*Fluka*). Isoselenocyanates **1a**–**1e** were prepared according to a slightly modified procedure of *Barton et al.* [29] starting from a formamide. Formanilide is commercially available (*Fluka* and *Aldrich*). *N*-(4-Chlorophenyl)-, *N*-(4-bromophenyl)-, *N*-(4-methylphenyl)-, and *N*-(4-methoxyphenyl)formamide were prepared from the respective aniline and 95% formic acid. The soln. was heated to reflux for 30 min and evaporated to

dryness in vacuo. The residue was dissolved in Et_2O and washed with diluted AcOH (5%), H_2O and aq. $NaHCO_3$ (5%). The aq. layer was extracted with Et_2O, the combined org. extracts were dried ($MgSO_4$) and evaporated. The crude products were purified by recrystallization from $EtOH/H_2O$.

3. *General Procedure for the Preparation of Selenadiazines* **3a**–**3f**: A 25 ml round-bottom flask equipped with a magnetic stirrer and condenser was charged with a mixture of an isoselenocyanate (1.0 mmol) and a phenacyl halide (1.0 mmol) in CH_2Cl_2 (20 ml). Then, hydrazine hydrate (0.05 ml, 1.0 mmol) was added in one portion, the mixture was stirred for 3 to 4 h at r.t. and evaporated to dryness i.v. The crude product was purified by CC on silica gel with hexane/AcOEt (100/0 to 50/50) as eluant.

*(Phenyl)(5-phenyl-3,6-dihydro-2*H*-[1,3,4]selenadiazin-2-yliden)amine* (**3a**). Yield: 226.3 mg (72%). Yellowish crystals. M.p. 186–188° (AcOEt). IR: 3443*m* (br.), 3150*w*, 3060*w*, 3034*w*, 2921*m* (br.) 1621*m*, 1580*s*, 1556v*s*, 1494*m*, 1471*w*, 1404*w*, 1303*w*, 1251*w*, 1209*m*, 1172*w*, 1137*w*, 1112*w*, 1075*w*, 1004*w*, 899*w*, 845*w*, 798*w*, 766*w*, 753*m*, 687*m*, 632*m*. ^{1}H-NMR: 3.95 (*s*, CH_2); 6.95–7.25 (br. *m*, *t*-like at 7.12, J = 7.4, 3 arom. H); 7.37 (*t*-like, J = 7.7, 2 arom. H); 7.45–7.55 (*m*, 3 arom. H); 7.91 (*d*-like, J = 7.7, 2 arom. H); 11.28 (br. *s*, NH). ^{13}C-NMR: 15.1 (*t*, CH_2); 123.1 (*d*, 1 arom. CH); 126.1 (*d*, 2 arom. CH); 128.4 (*d*, 3 arom. CH); 128.5 (*d*, 2 arom. CH); 129.2 (*d*, 2 arom. CH); 135.4, 149.0, 155.2 (3*s*, 2 arom. C, C(5)); 163.5 (*s*, C(2)). CI-MS: 318 (19), 317 (17), 316 (100, $[M(^{80}Se)+1]^+$), 315 (10), 314 (48), 313 (19), 312 (18), 239 (7), 238 (41, $[M–Ph]^+$), 236 (20), 225 (7). Anal. calc. for $C_{15}H_{13}N_3Se$ (314.25): C 57.33, H 4.17, N 13.37; found: C 57.34, H 4.03, N 13.09.

Crystals suitable for the X-ray crystal-structure determination were grown from $CHCl_3$/MeOH by slow evaporation of the solvent.

*(4-Bromophenyl)(5-phenyl-3,6-dihydro-2*H*-[1,3,4]selenadiazin-2-yliden)amine* (**3b**). Yield: 267.3 mg (68%). Yellowish crystals. M.p. 179–181° (AcOEt). IR: 3443*m* (br.), 3133*w*, 3056*w*, 2917*m* (br), 1623*m*, 1587v*s*, 1567*s*, 1490*m*, 1472*m*, 1444*m*, 1403*m*, 1297*w*, 1276*w*, 1214*s*, 1173*m*, 1105*w*, 1072*m*, 1003*w*, 889*m*, 841*m*, 827*s*, 759*s*, 693*s*, 658*m*, 632*w*. ^{1}H-NMR: 3.93 (*s*, CH_2); 6.70–7.00 (br. *m*, 2 arom. H); 7.45–7.60 (*m*, 5 arom. H); 7.85–8.00 (*m*, 2 arom. H); 11.71 (br. *s*, NH). ^{13}C-NMR: 15.3 (*t*, CH_2); 121.6 (*s*, 1 arom. C); 126.2 (*d*, 2 arom. CH); 128.5 (*d*, 3 arom. CH); 129.3 (*d*, 2 arom. CH); 131.3 (*d*, 2 arom. CH); 135.3, 148.0, 154.3 (3*s*, 2 arom. C, C(5)); 166.2 (*s*, C(2)). CI-MS: 398 (13), 397 (14), 396 (77), 395 (21), 394 (100, [*M*(^{80}Se,^{79}Br)+1]$^{+}$), 393 (21), 392 (47), 391 (14), 390 (14). Anal. calc. for $C_{15}H_{12}N_3SeBr$ (393.15): C 45.83, H 3.08, N 10.69; found: C 45.46, H 3.21, N 10.42.

*(4-Chlorophenyl)(5-phenyl-3,6-dihydro-2*H*-[1,3,4]selenadiazin-2-yliden)amine* (**3c**). Yield: 191.8 mg (55%). Yellowish crystals. M.p. 178–180° (AcOEt). IR: 3444*m* (br.), 3125*w*, 3047*w*, 2908*m* (br.), 2866*m* (br.), 1623*m*, 1584v*s*, 1568*s*, 1491*s*, 1473*m*, 1444*w*, 1403*m*, 1297*w*, 1277*w*, 1214*s*, 1178*w*, 1172*m*, 1107*w*, 1093*m*, 1071*w*, 1003*w*, 888*m*, 843*w*, 830*m*, 796*w*, 760*m*, 694*m*, 683*w*, 662*w*. ^{1}H-NMR: 3.95 (*s*, CH_2); 6.80–7.05 (br. *m*, 2 arom. H); 7.45 (*d*-like, *J* = 8.4, 2 arom. H); 7.50–7.60 (*m*, 3 arom. H); 7.90–8.05 (*m*, 2 arom. H); 11.64 (br. *s*, NH). ^{13}C-NMR: 15.3 (*t*, CH_2); 126.2 (*d*, 2 arom. CH); 128.4 (*d*, 2 arom. CH); 128.5 (*d*, 3 arom. CH); 129.3 (*s*, 2 arom. CH); 135.0, 135.3, 147.5, 155.3 (4*s*, 3 arom. C, C(5)); 163.9 (*s*, C(2)). CI-MS: 354 (6), 353 (8), 352 (44), 351 (18), 350 (100, [*M*(^{80}Se,^{35}Cl)+1]$^{+}$), 349 (15), 348 (48), 347 (17), 346 (17). Anal. calc. for $C_{15}H_{12}N_3SeCl$ (348.69): C 51.67, H 3.47, N 12.05; found: C 51.51, H 3.74, N 11.73.

*(4-Methoxyphenyl)(5-phenyl-3,6-dihydro-2*H*-[1,3,4]selenadiazin-2-yliden)amine* (**3d**). Yield: 229.3 mg (67%). Yellowish crystals. M.p. 132–134° (AcOEt). IR: 3439*m* (br.), 3346*m*, 2912*m* (br.), 2836*w*, 1654*s*, 1638*m*, 1580v*s*, 1544*s*, 1509v*s*, 1447*w*, 1282*m*, 1249*s*,

1211*w*, 1178*w*, 1109*w*, 1077*w*, 1033*w*, 1011*w*, 892*w*, 826*m*, 800*w*, 757*w*, 713*m*, 692*w*. ^{1}H-NMR: 3.82 (*s*, MeO); 3.90 (*s*, CH_2); 6.90–7.20 (br. *m*, *d*-like at 6.92, *J* = 8.2, 4 arom. H); 7.30–7.55 (*m*, 2 arom. H); 7.75–8.00 (*m*, 2 arom. H); 11.82 (br. *s*, NH). ^{13}C-NMR: 15.1 (*t*, CH_2); 55.4 (*q*, MeO); 115.6 (*d*, 2 arom. CH); 124.2 (*d*, 2 arom. CH); 128.3 (*d*, 2 arom. CH); 129.2 (*d*, 2 arom. CH); 131.1 (*d*, 1 arom. CH); 133.9, 147.8, 153.7, 158.4 (4*s*, 3 arom. C, C(5)); 166.1 (*s*, C(2)). CI-MS: 350 (8), 349 (12), 348 (65), 347 (21), 346 (100, [*M*(^{80}Se)+1]$^{+}$), 345 (19), 344 (52), 343 (15), 342 (14). Anal. calc. for $C_{16}H_{15}N_3OSe$ (344.28): C 55.82, H 4.39, N 12.21; found: C 55.95, H 4.67, N 12.23.

*(4-Bromophenyl)[5-(4-bromophenyl)-3,6-dihydro-2*H*-[1,3,4]selenadiazin-2-yliden]amine* (**3e**). Yield: 377.6 mg (80%). Yellowish crystals. M.p. 176–178° (AcOEt). IR: 3442*m* (br.), 3155*w*, 3051*w*, 2920*m* (br.), 1626*m*, 1590v*s*, 1576*s*, 1554*m*, 1485*m*, 1407*w*, 1299*w*, 1271*w*, 1209*m*, 1172*m*, 1146*w*, 1101*w*, 1070*m*, 1000*m*, 890*w*, 828*m*, 725*w*, 707*w*, 653*w*, 604*w*. ^{1}H-NMR: 3.88 (*s*, CH_2); 6.85–7.10 (br. *m*, 2 arom. H); 7.68 (*d*-like , *J* = 8.2, 2 arom. H); 7.80 (*d*-like, *J* = 8.2, 2 arom. H); 7.90–8.00 (*m*, 2 arom. H); 11.79 (br. *s*, NH). ^{13}C-NMR: 15.0 (*t*, CH_2); 122.8 (*s*, 2 arom. C); 124.2 (*d*, 2 arom. CH); 128.1 (*d*, 2 arom. CH); 131.3 (*d*, 2 arom. CH); 131.5 (*d*, 2 arom. CH); 134.5, 147.2, 155.5 (3*s*, 2 arom. C, C(5)); 162.9 (*s*, C(2)). CI-MS: 478 (7), 477 (9), 476 (52), 475 (19), 474 (100, [*M*(^{80}Se,^{81}Br,^{79}Br)+1]$^{+}$), 473 (23), 472 (85, [*M*(^{80}Se,^{79}Br,^{79}Br)+1]$^{+}$), 471 (19), 470 (35), 469 (8), 468 (9). Anal. calc. for $C_{15}H_{11}N_3SeBr_2$ (472.05): C 38.17, H 2.35, N 8.90; found: C 38.01, H 2.54, N 8.60.

*[5-(4-Bromophenyl)-3,6-dihydro-2*H*-[1,3,4]selenadiazin-2-ylidene](4-methylphenyl)amine* (**3f**). Yield: 317.5 mg (78%). Yellowish crystals. M.p. 202–204° (AcOEt). IR: 3441*m* (br.), 2919*m*, 2853*m* (br.), 1623*m*, 1583v*s*, 1554*m*, 1508*w*, 1486*w*, 1406*w*, 1269*w*, 1221*m*, 1173*m*, 1075*m*, 999*w*, 890*w*, 826*m*. ^{1}H-NMR: 2.40 (*s*, Me); 3.93 (*s*,

CH_2); 6.90–7.20 (*m*, 2 arom. H); 7.24 (*d*-like, *J* = 8.1, 2 arom. H); 7.52 (*d*-like, *J* = 8.1, 2 arom. H); 7.66 (*d*-like, *J* = 8.1, 2 arom. H); 11.50 (br. *s*, NH). ^{13}C-NMR: 14.8 (*t*, CH_2); 20.3 (*q*, Me); 121.6 (*s*, 1 arom. C); 122.6 (*d*, 2 arom. CH); 128.0 (*d*, 2 arom. CH); 129.0 (*d*, 2 arom. CH); 131.4 (*d*, 2 arom. CH); 134.7, 145.6, 155.0 (3*s*, 3 arom. C, C(5)); 163.2 (C(2)). CI-MS: 412 (13), 411 (15), 410 (77), 409 (33), 408 (100, $[M(^{80}Se,^{79}Br)+1]^+$), 407 (40), 406 (50), 405 (23), 404 (17). Anal. calc. for $C_{16}H_{14}N_3SeBr$ (407.07): C 47.20, H 3.47, N 10.32; found: C 46.72, H 3.51, N 10.15.

X-Ray Crystal-Structure Determination of **3a** (see *Table* and *Figure*)[3]). All measurements were made on a *Nonius KappaCCD* diffractometer [35] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. Data reduction was performed with *HKL Denzo* and *Scalepack* [36]. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method [37] was applied. Equivalent reflections were merged. Data collection and refinement parameters are given in the *Table*, and a view of the molecule is shown in the *Figure*. The structure was solved by direct methods using SIR92 [38], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. The amine H-atom was placed in the position indicated by a difference electron density map and its position was allowed to refine together with an isotropic displacement parameter. All of the remaining H-atoms were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic

[3]) CCDC-601303 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.

displacement parameter with a value equal to $1.2U_{eq}$ of its parent C-atom. Refinement of the structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2-F_c^2)^2$. A correction for secondary extinction was applied. One reflection, whose intensity was considered to be an extreme outlier, was omitted from the final refinement. Neutral atom scattering factors for non-H-atoms were taken from [39a], and the scattering factors for H-atoms were taken from [40]. Anomalous dispersion effects were included in F_c [41]; the values for f' and f'' were those of [39b]. The values of the mass attenuation coefficients are those of [39c]. All calculations were performed using the SHELXL97 [42] program.

REFERENCES

[1] M. Koketsu, H. Ishihara, *Curr. Org. Chem*. **2003**, *7*, 175.

[2] M. Morvan, G. Nadler, R. G. Zimmermann, *J. Heterocycl. Chem*. **1991**, *28*, 1365.

[3] J. Sibor, W.-D. Pfeiffer, A. Hetzheim, P. Pazdera, *Scripta Chem.* **1998**, *27-28*, 33; *Chem. Abstr*. **1999**, *132*, 23022.

[4] a) J. Liebscher, H. Hartmann, *Ger. Patent*, 1977, DD126309; *Chem. Abstr*. **1978**, *88*, 62425; b) W.-D. Pfeiffer, H. Rossberg, E. Bulka, *Ger. Patent*, 1983, DD203541; *Chem. Abstr*. **1984**, *100*, 156644; c) W.-D. Pfeiffer, E. Bulka, *Ger. Patent*, 1986, DD234678; *Chem. Abstr*. **1986**, *105*, 226667; d) W.-D. Pfeiffer, E. Bulka, *Ger. Patent*, 1991, DD290012; *Chem. Abstr*. **1991**, *115*, 183376.

[5] a) I. Shibuya, H. Nakanishi, *Bull. Chem. Soc. Jpn*. **1987**, *60*, 2686; b) R. N. Butler, A. Fox, *J. Chem. Soc., Perkin Trans. 1* **2001**, 394.

[6] H. G. Grant, L. A. Summers, *Z. Naturforsch. B, Anorg. Chem*. **1978**, *33*, 118.

[7] a) A. Gieren, V. Lamm, R. C. Haddon, M. L. Kaplan, *J. Am. Chem. Soc*. **1980**, *102*, 5070; b) J. P. Boutique, J. Riga, J. J. Verbist, J. Delhalle, J. G. Fripiat, J. M. Andre, R. C. Haddon, M. L. Kaplan, *J. Am. Chem. Soc*. **1982**, *104*, 2691; c) A. Haas, E. Hoppmann, V. M. Karpov, V. E. Platonov, M. M. Shakirov, *J. Fluorine Chem.* **2000**, *102*, 313.

[8] M.-C. Forest, P. Lahouratate, M. Martin, G. Nadler, M. J. Quiniou, R. G. Zimmermann, *J. Med. Chem*. **1992**, *35*, 163.

[9] W.-D. Pfeiffer, E. Bulka, *Ger. Patent*, 1990, DD281582, *Chem. Abstr*. **1991**, *114*, 185571.

[10] I. Shibuya, H. Nakanishi, *Jap. Patent*, 1987, JP62106088; *Chem. Abstr*. **1988**, *108*, 221705.

[11] E. Bulka, *Chem. Scr*. **1975**, *8A*, 39; *Chem. Abstr.* **1976**, *85*, 21162.

[12] a) B. Marcewicz-Rojewska, S. Bilinski, *Acta Polon. Pharm*. **1980**, *2*, 169; b) S. Bilinski, L. Bielak, J. Chmielewski, B. Marcewicz-Rojewska, I. Musik, *Acta Polon. Pharm*. **1989**, *4*, 343.

[13] a) V. A. Bobylev, M. L. Petrov, V. N. Chistokletov, A. A. Petrov, *J. Org. Chem. USSR* **1982**, *18*, 200; b) M. L. Petrov, M. A. Abramov, V. A. Galishev, A. A. Petrov, *J. Org. Chem. USSR* **1989**, *25*, 181.

[14] a) H. Rossberg, W.-D. Pfeiffer, E. Bulka, *Wiss. Z. Ernst-Moritz-Arndt-Univ. Greifswald, Math.-nat.wiss. Reihe*, **1985**, *34*, 75; b) W.-D. Pfeiffer, J. Buhrow, E. Bulka, *Wiss. Z. Ernst-Moritz-Arndt-Univ. Greifswald, Math.-nat.wiss. Reihe*, **1988**, *37*, 38; c) W.-D. Pfeiffer, E. Bulka, *Chem. Zeitung* **1991**, *115,* 361; d) T. Jira, W.-D. Pfeiffer, K. Lachmann, U. Epperlein, *Pharmazie* **1994**, *49*, 401; e) W.-D. Pfeiffer, H.

Rossberg, *Pharmazie* **1997**, *48*, 732; f) T. Jira, A. Stelzer, W.-D. Pfeiffer, C. Schopplich, S. Siegert, M. Kindermann, *Pharmazie* **1997**, *52*, 831.

[15] a) H. Schubert, J. Bleichert, *Z. Chem*. **1963**, *9*, 349; b) K. Szulzewski, W.-D. Pfeiffer, E. Bulka, H. Rossberg, B. Schulz, *Acta Chem. Scand.* **1993**, *47*, 302.

[16] a) Y. V. Zachinyaev, A. I. Bobrov, *Ukr. Khim. Zh.*, **1988**, *54,* 538; *Chem. Abstr*. **1989**, *110*, 212778; b) Y. V. Zachinyaev, A. I. Bobrov, A. I. Ginak, *Rev. Roum. Chim.* **1989**, *34,* 901; *Chem. Abstr*. **1990**, *112*, 77132.

[17] Y. Zhou, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 539.

[18] Y. Zhou, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2000**, *83*, 1576.

[19] P. K. Atanassov, Y. Zhou, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2002**, *85*, 1102.

[20] P. K. Atanassov, A. Linden, H. Heimgartner, *Heterocycles* **2003**, *61*, 569.

[21] P. K. Atanassov, A. Linden, H. Heimgartner, *Heterocycles* **2004**, *62*, 521.

[22] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2004**, *87*, 1452.

[23] P. K. Atanassov, A. Linden, H. Heimgartner, *Helv. Chim. Acta* **2004**, *87*, 1873.

[24] P. K. Atanassov, A. Linden, H. Heimgartner, *J. Sulfur Chem.* **2006**, in press.

[25] G. L. Sommen, A. Linden, H. Heimgartner, *Helv. Chim. Acta*, **2005**, *88*, 766.

[26] G. L. Sommen, A. Linden, H. Heimgartner, *Eur. J. Org. Chem.* **2005**, *14*, 3128.

[27] G. L. Sommen, A. Linden, H. Heimgartner, *Tetrahedron*, **2005**, *in press*.

[28] G.L. Sommen, A. Linden, H. Heimgartner, *Tetrahedron Lett.* **2005**, *46*, 6723.

[29] a) D. H. R. Barton, S. I. Parekh, M. Tajbakhsh, E. A. Theodorakis, C.-L. Tse *Tetrahedron*, **1994**, *50*, 639; b) M. T. Bakhsh, Y. S. Behshtiha, M. M. Heravi *J. Chem. Soc. Pakistan* **1996**, *18*, 159.

[30] C. K. Johnson, 'ORTEP II', Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.

[31] J. Bernstein, R. E. Davis, L. Shimoni, N.-L. Chang, *Angew. Chem. Int. Ed.* **1995**, *34*, 1555.

[32] J. E. Baldwin, *J. Chem. Soc., Chem. Commun.* **1976**, 734.

[33] G. L. Sommen, A. Linden, H. Heimgartner, *Heterocycles* **2005**, *65*, 1903.

[34] F. Favero, G. L. Sommen, A. Linden, H. Heimgartner, *Heterocycles* **2006**, *67*, 749.

[35] R. Hooft, *KappaCCD Collect Software*, Nonius BV, Delft, The Netherlands, 1999.

[36] Z. Otwinowski, W. Minor, in *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, Eds. C. W. Carter Jr., R. M. Sweet, Academic Press, New York, 1997, p. 307.

[37] R. H. Blessing, *Acta Crystallogr., Sect A* **1995**, *51*, 33.

[38] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *SIR92*, *J. Appl. Crystallogr.* **1994**, *27*, 435.

[39] a) E. N. Maslen, A. G. Fox, M. A. O'Keefe, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477; b) D. C. Creagh, W. J. McAuley, *ibid*. Table 4.2.6.8, p. 219; c) D. C. Creagh, J. H. Hubbell, *ibid*. Table 4.2.4.3, p. 200.

[40] R. F. Stewart, E. R. Davidson, W. T. Simpson, *J. Chem. Phys.* **1965**, *42*, 3175.

[41] J. A. Ibers, W. C. Hamilton, *Acta Crystallogr.* **1964**, *17*, 781.

[42] G. M. Sheldrick, *SHELXL97, Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, 1997.

Table 1. *Preparation of Selenadiazines* **3** *from Isoselenocyanates* **1**

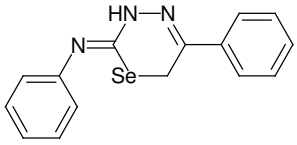
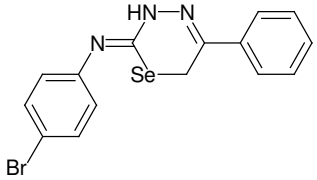
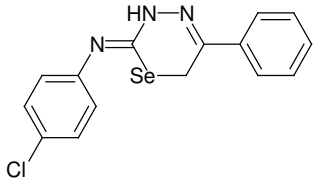
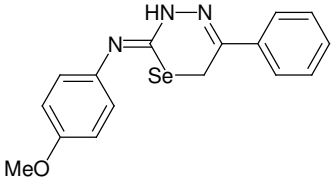
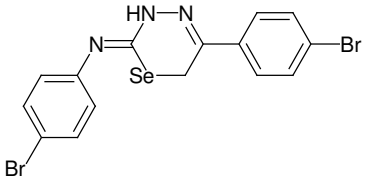
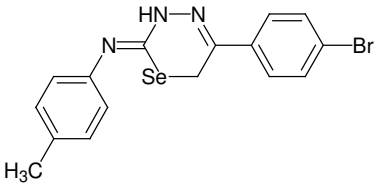
Entry	**1**	R^1	**2**	R^2	Selenadiazines **3**	Yield (%)
1	**a**	Ph	**a**	Ph	**a** 	72
2	**b**	4-BrC_6H_4	**a**	Ph	**b** 	68
3	**c**	4-ClC_6H_4	**a**	Ph	**c** 	55
4	**d**	4-$MeOC_6H_4$	**a**	Ph	**d** 	67
5	**b**	4-BrC_6H_4	**b**	4-BrC_6H_4	**e** 	80
6	**e**	4-MeC_6H_4	**b**	4-BrC_6H_4	**f** 	78

Table 2. *Crystallographic Data of Compound* **3a**

Crystallized from		$CHCl_3$/MeOH
Empirical formula		$C_{15}H_{13}N_3Se$
Formula weight [g mol^{-1}]		314.19
Crystal color, habit		pale-yellow, prism
Crystal dimensions [mm]		0.18 × 0.23 × 0.28
Temperature [K]		160(1)
Crystal system		monoclinic
Space group		$P2_1/n$
Z		4
Reflections for cell determination		27519
2θ range for cell determination [°]		4–60
Unit cell parameters	a [Å]	10.5899(2)
	b [Å]	8.7839(1)
	c [Å]	15.2309(3)
	β [°]	110.2058(9)
	V [Å^3]	1329.60(4)
D_x [g cm^{-3}]		1.569
μ(MoK_α) [mm^{-1}]		2.811
Scan type		ϕ and ω
$2\theta_{(max)}$ [°]		60
Transmission factors (min; max)		0.510; 0.623
Total reflections measured		37327
Symmetry independent reflections		3883
Reflections with $I > 2\sigma(I)$		3316
Reflections used in refinement		3882
Parameters refined		177
Final $R(F)$ [$I > 2\sigma(I)$ reflections]		0.0297
$wR(F^2)$ (all data)		0.0750
Weights: $w = [\sigma^2(F_o^2) + (0.0359P)^2 + 0.9122P]^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$		
Goodness of fit		1.033
Secondary extinction coefficient		0.0036(8)
Final Δ_{max}/σ		0.002
$\Delta\rho$ (max; min) [e Å^{-3}]		0.64; -0.50